Serial No.: 08/956,518 MC File No.: UTC-03042 By: KTM

In The Matter of the Application Of: SHERRY LEONARD et al.

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Sherry Leonard *et al.*
Serial No.: 08/956,518 Group No.: 1645
Filed: 10/23/97 Examiner: R. Hayes
Entitled: **ALPHA-7 NICOTINIC RECEPTOR**

INFORMATION DISCLOSURE STATEMENT TRANSMITTAL

Assistant Commissioner for Patents
Washington, D.C. 20231

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Sir:

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Dated: March 30, 1999

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PATENT
Attorney Docket No. **UTC-3042**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Sherry Leonard *et al.*
Serial No.: 08/956,518 Group No.: 1645
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By: Marlene Gaitano
Marlene Gaitano

Sir:

The citations listed below, copies attached, may be material to the examination of the above-identified application, and are therefore submitted in compliance with the duty of disclosure defined in 37 C.F.R. §§ 1.56 and 1.97. The Examiner is requested to make these citations of official record in this application.

The following printed publications are referred to in the body of the specification:

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- U.S. Patent No. 5,580,859 to Felgner *et al.*;
- U.S. Patent No. 5,459,127 to Felgner *et al.*;
- U.S. Patent No. 5,399,346 to Anderson *et al.*;
- U.S. Patent No. 5,322,770 to Gelfand;
- U.S. Patent No. 5,124,263 to Temin *et al.*;
- U.S. Patent No. 4,980,289 to Temin *et al.*;
- U.S. Patent No. 4,965,188 to Mullis;
- U.S. Patent No. 4,946,778 to Ladner *et al.*;
- U.S. Patent No. 4,861,719 to Miller;
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- Vinogradova *et al.*, "Do Semantic Priming Effects Correlate with Sensory Gating in Schizophrenia," *Biol. Psychiat.* 39: 821-824 (1996);
- Vinogradova, in *The Hippocampus 2: Neurophysiology and Behavior*, Issacson and Pribram (eds.), pp. 3-69, Plenum Press, New York, New York (1975);
- von Heijne, "A new method for predicting signal sequence cleavage sites," *Nucl. Acids Res.* 14: 4683-4690 (1986);
- Voss *et al.*, "The role of enhancers in the regulation of cell-type-specific transcriptional control," *Trends Biochem. Sci.* 11:287-289 [1986];
- Wada *et al.*, "Distribution of Alpha2, Alpha3, Alpha4, and Beta2 Neuronal Nicotinic Receptor Subunit mRNAs in the Central Nervous System: A Hybridization Histochemical Study in the Rat," *J. Compar. Neurol.* 284: 314-335 (1989);
- Waldo *et al.*, "Codistribution of a Sensory Gating Deficit and Schizophrenia in Multi-affected Families," *Psychiat. Res.* 39: 257-268 (1991);
- Waldo *et al.*, "Auditory sensory gating, hippocampal volume, and catecholamine metabolism in schizophrenics and their siblings," *Schizophr. Res.* 12: 93-106 (1991);
- Wang *et al.*, "Evidence for a susceptibility locus for schizophrenia on chromosome 6pter-p22," *Nature Genet.* 10: 41-46 (1995);
- Williams *et al.*, "Introduction of foreign genes into tissues of living mice by DNA-coated microprojectiles," *Proc. Natl. Acad. Sci. U.S.A.* 88: 2726-2730 (1991);
- Wilson *et al.*, "Habituation of Human Limbic Neuronal Response to Sensory Stimulation," *Exp. Neurol.* 84: 74-97 (1984);

- Wilson *et al.*, "Hepatocyte-directed Gene Transfer in Vivo Leads to Transient Improvement of Hypercholesterolemia in Low Density Lipoprotein Receptor-deficient Rabbits," *J. Biol. Chem.* 267: 963-967 (1992);
- Wonnacott, "α-Bungarotoxin Binds to Low-Affinity Nicotine Binding Sites in Rat Brain," *J. Neurochem.* 47: 1706-1712 (1986);
- Wu and Wallace, "The Ligation Amplification Reaction (LAR) -- Amplification of Specific DNA Sequences Using Sequential Rounds of Template-Dependent Ligation," *Genomics* 4:560-569 [1989];
- Wu and Wu, "Receptor-mediated Gene Delivery and Expression in Vivo," *J. Biol. Chem.* 263: 14621-14624 (1988);
- Wu and Wu, "Receptor-mediated *in Vitro* Gene Transformation by a Soluble DNA Carrier System," *J. Biol. Chem.* 262: 4429-4432 (1987); and
- Zhang *et al.*, "Neuronal Acetylcholine Receptors That Bind α-Bungarotoxin with High Affinity Function as Ligand-Gated Ion Channels," *Neuron* 12: 167-177 (1994).

Applicants have become aware of the following printed publications which may be material to the examination of this application:

- Doucette-Stamm *et al.*, "Cloning and Sequence of the Human α7 Nicotinic Acetylcholine Receptor," *Drug Dev. Res.* 30: 252-256 (1993) disclose the isolation and sequence of clones corresponding to the human α_7 nicotinic acetylcholine receptor. Unlike the presently claimed invention, Doucette-Stamm *et al.* do not disclose isolated fragments of the human α_7 sequence, encoded by SEQ ID Nos. 85-103 of the presently claimed invention. Furthermore, Doucette-Stamm *et al.* do not disclose methods for detection of a polynucleotide encoding α_7 in a biological sample, comprising the step of hybridizing fragments of the α_7 sequence encoded by SEQ ID Nos. 9-11 and 84-103 of the presently claimed invention to nucleic acid of the biological sample; nor do Doucette-Stamm *et al.* disclose methods for amplification of nucleic acid from a sample suspected of containing nucleic acid encoding α_7,

using at least two primers selected from SEQ ID Nos. 1-8 and 12-83 of the presently claimed invention;

- Chini *et al.*, "Molecular Cloning and Chromosomal Localization of the Human α7-Nicotinic Receptor Subunit Gene (CHRNA7)," *Genomics* 19: 379-381 (1994) disclose nucleotide and amino acid sequences for the human α7 neuronal nicotinic subunit for chromosome 15, band q14 region. Unlike the presently claimed invention, Chini *et al.* do not disclose isolated fragments of the α_7 sequence encoded by SEQ ID Nos. 84-103 of the presently claimed invention. Furthermore, Chini *et al.* do not disclose methods for detection of a polynucleotide encoding α_7 in a biological sample, comprising the step of hybridizing fragments of the α_7 sequence encoded by SEQ ID Nos. 9-11 and 84-103 of the presently claimed invention to nucleic acid of the biological sample; nor do Chini *et al.* disclose methods for amplification of nucleic acid from a sample suspected of containing nucleic acid encoding α_7, using at least two primers selected from SEQ ID Nos. 1-8 and 12-83 of the presently claimed invention;
- Garcia-Guzman *et al.*, "α-Bungarotoxin-sensitive Nicotinic Receptors on Bovine Chromaffin Cells: Molecular Cloning, Functional Expression and Alternative Splicing of the α7 Subunit," *Eur. J. Neurosci.* 7: 647-655 (1995) disclose that α-bungarotoxin-sensitive acetylcholine receptors from bovine chromaffin cells contain an α_7 subunit homologous to those previously cloned from chicks, rats and humans, and show alternative splicing of the α_7 subunit transcript. Garcia-Guzman *et al.* do not disclose isolated fragments of the α_7 sequence encoded by SEQ ID Nos. 84-103 of the presently claimed invention. Furthermore, Garcia-Guzman *et al.* do not disclose methods for detection of a polynucleotide encoding α_7 in a biological sample, comprising the step of hybridizing fragments of the α_7 sequence encoded by SEQ ID Nos. 9-11 and 84-103 of the presently claimed invention to nucleic acid of the biological sample; nor do Garcia-Guzman *et al.* disclose methods for amplification of nucleic acid from a sample suspected of containing nucleic acid encoding α_7,

using at least two primers selected from SEQ ID Nos. 1-8 and 12-83 of the presently claimed invention;

- Anand and Lindstrom, "Nucleotide sequence of the human nicotinic acetylcholine receptor β2 subunit gene," *Nuc. Acids Res.* 18: 4272 (1990) disclose the nucleotide sequence of human acetylcholine receptor β_2 subunit gene. Unlike the presently claimed invention, Anand and Lindstrom do not disclose isolated nucleotide sequences encoding a portion of the human α_7 nicotinic receptor. Furthermore, Anand and Linstrom do not disclose methods for detection of a polynucleotide encoding α_7 in a biological sample, nor do Anand and Linstrom disclose methods for amplification of nucleic acid from a sample suspected of containing nucleic acid encoding α_7;
- Deneris *et al.*, "Primary Structure and Expression of β2: A Novel Subunit of Neuronal Nicotinic Acetylcholine Receptors," *Neuron* 1: 45-54 (1988) disclose the β2 subunit of the neuronal receptor family. Unlike the presently claimed invention, Deneris *et al.* do not disclose isolated nucleotide sequences encoding a portion of the human α_7 nicotinic receptor. Furthermore, Deneris *et al.* do not disclose methods for detection of a polynucleotide encoding α_7 in a biological sample, nor do Deneris *et al.* disclose methods for amplification of nucleic acid from a sample suspected of containing nucleic acid encoding α_7;
- Fornasari *et al.*, "Structural and Functional Characterization of the Human α3 Nicotinic Subunit Gene Promoter," *Mol. Pharmacol.* 51: 250-261 (1997) disclose the structural and functional features of the human α_3 nicotinic receptor subunit promoter, and investigate the tissue-specific activity of the human α_3 gene 5' regulatory sequences. Unlike the presently claimed invention, Fornasari *et al.* do not disclose isolated nucleotide sequences encoding a portion of the human α_7 nicotinic receptor. Furthermore, Fornasari *et al.* do not disclose methods for detection of a polynucleotide encoding α_7 in a biological sample, nor do Fornasari *et al.* disclose methods for amplification of nucleic acid from a sample suspected of containing nucleic acid encoding α_7; and

- Fornasari *et al.*, "Molecular cloning of human neuronal nicotinic receptor α3-subunit," *Neurosci. Lett.* 111: 351-356 (1990) disclose a protein showing high homology to rat α_3 neuronal nicotinic receptor, and identify this protein as the human α_3-nicotinic subunit. Unlike the presently claimed invention, Fornasari *et al.* do not disclose isolated nucleotide sequences encoding a portion of the human α_7 nicotinic receptor. Furthermore, Fornasari *et al.* do not disclose methods for detection of a polynucleotide encoding α_7 in a biological sample, nor do Fornasari *et al.* disclose methods for amplification of nucleic acid from a sample suspected of containing nucleic acid encoding α_7.

Applicants have included the following publications in which the inventors are co-authors. These publications, while not prior art, have been included for completeness:

- Gault *et al.*, "Genomic Organization and Partial Duplication of the Human α7 Neuronal Nicotinic Acetylcholine Receptor Gene (CHRNA7), *Genomics* 52: 173-185 (1998) disclose the cloning, sequencing, and characterization of a putative promoter 5' of the translation start in exon 1 of the human α_7 neuronal nicotinic acetyl receptor gene;
- Leonard *et al.*, "Linkage of a chromosome 15 locus to a neurophysiological deficit in schizophrenia," *Am. J. Human Genet.* 59: A225 (1996) investigate an inhibitory neuronal mechanism which regulates response to auditory stimuli, and suggest that the α_7 neuronal nicotinic receptor is a candidate gene in this pathway. Unlike the presently claimed invention, Leonard *et al.* do not disclose isolated nucleotide sequences encoding a portion of the human α_7 nicotinic receptor. Furthermore, Leonard *et al.* do not disclose methods for detection of a polynucleotide encoding α_7 in a biological sample, nor do Leonard *et al.* disclose methods for amplification of nucleic acid from a sample suspected of containing nucleic acid encoding α_7;
- Breese *et al.*, "Comparison of the Regional Expression of Nicotinic Acetylcholine Receptor α7 mRNA and [^{125}I]-α-bungarotoxin binding in Human Postmortem Brain," *J. Comp. Neurol.* 387: 385-398 (1997) compare the expression of α_7 mRNA and the localization of bungarotoxin binding sites in

human brain. Unlike the presently claimed invention, Breese *et al.* do not disclose isolated nucleotide sequences encoding a portion of the human α_7 nicotinic receptor. Furthermore, Breese *et al.* do not disclose methods for detection of a polynucleotide encoding α_7 in a biological sample, nor do Breese *et al.* disclose methods for amplification of nucleic acid from a sample suspected of containing nucleic acid encoding α_7;

- Leonard *et al.*, "Genomic Structure of the Human α7 Neuronal Nicotinic Acetylcholine Receptor Subunit," *Abstracts, Society for Neuroscience*, 27th Annual Meeting, October 25-30 (1997) disclose the genomic structure for the human α_7 gene (*i.e.*, exon/intron borders, promoter, and 3'-UT sequence). Unlike the presently claimed invention, Leonard *et al.* do not disclose isolated nucleotide sequences encoding a portion of the human α_7 nicotinic receptor. Furthermore, Leonard *et al.* do not disclose methods for detection of a polynucleotide encoding α_7 in a biological sample, nor do Leonard *et al.* disclose methods for amplification of nucleic acid from a sample suspected of containing nucleic acid encoding α_7;
- Freedman *et al.*, "Linkage of a neurophysiological deficit in schizophrenia to a chromosome 15 locus," *Proc. Natl. Acad. Sci. U.S.A.* 94: 587-592 (1997) disclose that a defect in a neuronal mechanism which regulates response to auditory stimuli is linked to a dinucleotide polymorphism at chromosome 15q13-14, the site of the α_7 nicotinic receptor. Unlike the presently claimed invention, Freedman *et al.* do not disclose isolated nucleotide sequences encoding a portion of the human α_7 nicotinic receptor. Furthermore, Freedman *et al.* do not disclose methods for detection of a polynucleotide encoding α_7 in a biological sample, nor do Freedman *et al.* disclose methods for amplification of nucleic acid from a sample suspected of containing nucleic acid encoding α_7;
- Logel *et al.*, "Expression of High and Low Affinity Neuronal Nicotinic Receptors in Tissues of Neural Crest Origin," *Abstracts, Society for Neuroscience*, 27th Annual Meeting, October 25-30 (1997) investigate the expression of neuronal nicotine receptor subunits in cells of neural crest origin, and suggest that specific subunits of the neuronal nicotinic receptors are present

in peripheral tissues of neural crest origin. Unlike the presently claimed invention, Logel *et al.* do not disclose isolated nucleotide sequences encoding a portion of the human α_7 nicotinic receptor. Furthermore, Logel *et al.* do not disclose methods for detection of a polynucleotide encoding α_7 in a biological sample, nor do Logel *et al.* disclose methods for amplification of nucleic acid from a sample suspected of containing nucleic acid encoding α_7;

- Breese *et al.*, "Abnormal Regulation of High Affinity Nicotinic Receptor Binding in Schizophrenics," *Abstracts, Society for Neuroscience*, 27th Annual Meeting, October 25-30 (1997) disclose the possibility of an alteration in the regulation of high affinity nicotinic receptor expression by nicotine use in schizophrenia. Unlike the presently claimed invention, Breese *et al.* do not disclose isolated nucleotide sequences encoding a portion of the human α_7 nicotinic receptor. Furthermore, Breese *et al.* do not disclose methods for detection of a polynucleotide encoding α_7 in a biological sample, nor do Breese *et al.* disclose methods for amplification of nucleic acid from a sample suspected of containing nucleic acid encoding α_7;
- Gault *et al.*, "Contig construction across the 15q14 schizophrenia linkage region and candidate gene characterization of the partially duplicated α7 nicotinic receptor," *Am. J. Human Genet.* 63: A249 (1998) disclose the assembly of a contig across the 15q14 schizophrenia linkage region, which includes the α_7 nicotinic acetylcholine receptor gene, and investigate this region's linkage to the schizophrenia phenotype. Unlike the presently claimed invention, Gault *et al.* do not disclose isolated nucleotide sequences encoding a portion of the human α_7 nicotinic receptor. Furthermore, Gault *et al.* do not disclose methods for detection of a polynucleotide encoding α_7 in a biological sample, nor do Gault *et al.* disclose methods for amplification of nucleic acid from a sample suspected of containing nucleic acid encoding α_7;
- Leonard *et al.*, "Additional evidence for a chromosome 15 locus in schizophrenia: Analysis of affected sibpairs from the NMH genetics initiative," *Am. J. Human Genet.* 63: A297 (1998) investigate the presence of a dinucleotide-repeat marker, D15S1360, containing the coding region of α_7

neuronal nicotinic acetylcholine receptor gene in affected sibpairs from the NIMH genetics initiative. Unlike the presently claimed invention, Leonard *et al.* do not disclose isolated nucleotide sequences encoding a portion of the human α_7 nicotinic receptor. Furthermore, Leonard *et al.* do not disclose methods for detection of a polynucleotide encoding α_7 in a biological sample, nor do Leonard *et al.* disclose methods for amplification of nucleic acid from a sample suspected of containing nucleic acid encoding α_7;

- Leonard *et al.*, "Further Investigation of a Chromosome 15 Locus in Schizophrenia: Analysis of Affected Sibpairs From the NIMH Genetics Initiative," *Am. J. Med. Genet.* 81: 308-312 (1998) disclose that analysis of affected sibpairs from the NIMH Genetics Initiative shows a significant proportion of D15S1360 alleles shared identical-by-descent, and gives support for the involvement of this chromosomal locus in the genetic transmission of schizophrenia. Unlike the presently claimed invention, Leonard *et al.* do not disclose isolated nucleotide sequences encoding a portion of the human α_7 nicotinic receptor. Furthermore, Leonard *et al.* do not disclose methods for detection of a polynucleotide encoding α_7 in a biological sample, nor do Leonard *et al.* disclose methods for amplification of nucleic acid from a sample suspected of containing nucleic acid encoding α_7;
- Zetterström *et al.*, "Polymorphisms at the Calcitonin/CGRP-α Gene Locus: Investigation of Possible Associations with Neurological or Psychiatric Disease," *Abstracts, Society for Neuroscience*, 28th Annual Meeting, November 7-12 (1998) investigate possible associations of polymorphisms (*i.e.*, single nucleotide polymorphisms, deletion and missense mutation) with neurological or psychiatric diseases such as bipolar affective disorder, Parkinson's disease and schizophrenia. Unlike the presently claimed invention, Zetterström *et al.* do not disclose isolated nucleotide sequences encoding a portion of the human α_7 nicotinic receptor. Furthermore, Zetterström *et al.* do not disclose methods for detection of a polynucleotide encoding α_7 in a biological sample, nor do Zetterström *et al.* disclose methods for amplification of nucleic acid from a sample suspected of containing nucleic acid encoding α_7;

- Drebing *et al.*, "Expression of the Human α7 Neuronal Nicotinic Acetylcholine Receptor and a Partial Gene Duplication," *Abstracts, Society for Neuroscience*, 28th Annual Meeting, November 7-12 (1998) disclose that human α_7 neuronal nicotinic receptor can be detected in cycloheximide treated immortalized lymphocytes by ectopic PCR. Unlike the presently claimed invention, Drebing *et al.* do not disclose isolated nucleotide sequences encoding a portion of the human α_7 nicotinic receptor. Furthermore, Drebing *et al.* do not disclose methods for detection of a polynucleotide encoding α_7 in a biological sample, nor do Drebing *et al.* disclose methods for amplification of nucleic acid from a sample suspected of containing nucleic acid encoding α_7;
- Leonard *et al.*, "Genomic Organization and Partial Duplication of the Human α7 Neuronal Nicotinic Acetylcholine Receptor Subunit Gene," *Abstracts, Society for Neuroscience*, 28th Annual Meeting, November 7-12 (1998) disclose the cloning, sequencing, and characterization of a putative promoter 5' of the translation start in exon 1 of the human α_7 neuronal nicotinic acetyl receptor gene. Unlike the presently claimed invention, Leonard *et al.* do not disclose isolated nucleotide sequences encoding a portion of the human α_7 nicotinic receptor. Furthermore, Leonard *et al.* do not disclose methods for detection of a polynucleotide encoding α_7 in a biological sample, nor do Leonard *et al.* disclose methods for amplification of nucleic acid from a sample suspected of containing nucleic acid encoding α_7;
- Dudek *et al.*, "Expression in Human Brain of Novel Exons Associated with a Partial Duplication of the α7 Neuronal Nicotinic Receptor," *Abstracts, Society for Neuroscience*, 28th Annual Meeting, November 7-12 (1998) disclose that proximal to the full-length human α_7 neuronal nicotinic receptor subunit gene, exons 5 to 10 have been duplicated with intervening intron sequences, and four novel exons A, B, C and D were found 5' to exon 5 in the duplication clones. Unlike the presently claimed invention, Dudek *et al.* do not disclose isolated nucleotide sequences encoding a portion of the human α_7 nicotinic receptor. Furthermore, Dudek *et al.* do not disclose methods for detection of a polynucleotide encoding α_7 in a biological sample, nor do Dudek *et al.* disclose

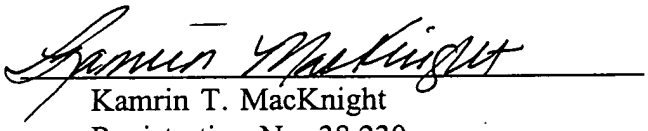
methods for amplification of nucleic acid from a sample suspected of containing nucleic acid encoding α_7;

- Breese *et al.*, "Abnormal Regulation of the High Affinity Nicotinic Receptors in Schizophrenia," *Abstracts, Society for Neuroscience*, 28th Annual Meeting, November 7-12 (1998) characterize [^{3}H]-epibatidine, a novel nicotinic receptor ligand in human postmortem brain, and give support that an abnormality in the regulation of the high affinity neuronal nicotinic receptors may be involved in the neuropathophysiology of schizophrenia through studies comparing nicotinic receptor binding in the cortex and caudate areas. Unlike the presently claimed invention, Breese *et al.* do not disclose isolated nucleotide sequences encoding a portion of the human α_7 nicotinic receptor. Furthermore, Breese *et al.* do not disclose methods for detection of a polynucleotide encoding α_7 in a biological sample, nor do Breese *et al.* disclose methods for amplification of nucleic acid from a sample suspected of containing nucleic acid encoding α_7;
- Lee *et al.*, "The Effect of Nicotine and Haloperidol on High Affinity Nicotinic Receptors and Dopamine D2 Receptors in the Rat Brain," *Abstracts, Society for Neuroscience*, 28th Annual Meeting, November 7-12 (1998) disclose that haloperidol has no effect on nicotine induced upregulation of nicotinic binding in rat, and suggest that decreased nicotine binding in brains of schizophrenic smokers is not due to chronic treatment with typical neuroleptics. Unlike the presently claimed invention, Lee *et al.* do not disclose isolated nucleotide sequences encoding a portion of the human α_7 nicotinic receptor. Furthermore, Lee *et al.* do not disclose methods for detection of a polynucleotide encoding α_7 in a biological sample, nor do Lee *et al.* disclose methods for amplification of nucleic acid from a sample suspected of containing nucleic acid encoding α_7; and
- Adler *et al.*, "Schizophrenia, Sensory Gating, and Nicotinic Receptors," *Schizophrenia Bulletin* 24: 189-202 (1998) summarize findings implicating the α_7-nicotinic receptor in schizophrenia, and discuss implications for the pathogenesis of schizophrenia that arise from studies of α_7-nicotinic receptor effects on cell growth and differentiation. Unlike the presently claimed

invention, Adler *et al.* do not disclose isolated nucleotide sequences encoding a portion of the human α_7 nicotinic receptor. Furthermore, Adler *et al.* do not disclose methods for detection of a polynucleotide encoding α_7 in a biological sample, nor do Adler *et al.* disclose methods for amplification of nucleic acid from a sample suspected of containing nucleic acid encoding α_7.

This Information Disclosure Statement under 37 C.F.R. §§ 1.56 and 1.97 is not to be construed as a representation that a search has been made, that additional information material to the examination of this application does not exist, or that any one or more of these citations constitutes prior art.

Dated: March 29, 1999



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FORM PTO-1449 (Modified)	U.S. Department of Commerce Patent and Trademark Office	Attorney Docket No.: UTC-03042	Serial No.: 08/956,518
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use Several Sheets If Necessary)		Applicant: Sherry Leonard *et al.*	
(37 CFR § 1.98(b))		Filing Date: 10/23/97	Group Art Unit: 1645

U.S. PATENT DOCUMENTS

Examiner Initials	Cite No.	Serial / Patent Number	Issue Date	Applicant / Patentee	Class	Subclass	Filing Date
	1	5,589,466	12/31/96	Felgner *et al.*			1/26/95
	2	5,580,859	12/3/96	Felgner *et al.*			3/18/94
	3	5,459,127	10/17/95	Felgner *et al.*			9/16/93
	4	5,399,346	3/21/95	Anderson *et al.*			3/30/94
	5	5,322,770	6/21/94	Gelfand			12/22/89
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	7	4,980,289	12/25/90	Temin *et al.*			4/27/87
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	11	4,683,202	7/28/87	Mullis			10/25/85
	12	4,683,195	7/28/87	Mullis *et al.*			2/7/86
	13	4,650,764	3/17/87	Temin *et al.*			3/26/84

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		Document Number	Publication Date	Country / Patent Office	Class	Subclass	Translation	
							Yes	No
	14	WO 96/25508	8/22/96	France				
	15	WO 96/17823	6/13/96	France				
	16	WO 95/21931	8/17/95	France				
	17	WO 95/18863	7/13/95	France				
	18	WO 96/15244	5/23/96	United States				
	19	WO 95/07358	3/16/95	United States				
	20	WO 95/02697	1/26/95	France				
	21	WO 94/26914	11/24/94	France				
	22	WO 94/21807	9/29/94	Great Britain				
	23	WO 93/03367	2/18/93	United States				
	24	WO 92/05263	4/2/92	Great Britain				
	25	WO 90/02806	3/22/90	United States				
	26	WO 90/13678	11/15/90	United States				
	27	WO 89/07150	8/10/89	United States				
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	29	EP 0178220 B1	4/16/86	European Patent Office				

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(37 CFR § 1.98(b))		Filing Date: 10/23/97	Group Art Unit: 1645

		OTHER DOCUMENTS (Including Author, Title, Date, Relevant Pages, Place of Publication)
	31	Adler *et al.*, " Normalization by Nicotine of Deficient Auditory Sensory Gating in the Relatives of Schizophrenics," *Biol. Psych.* 32: 607-616 (1992);
	32	Adler *et al.*, "Normalization of Auditory Physiology by Cigarette Smoking in Schizophrenic Patients," *Am. J. Psychol.* 150: 1856-1861 (1993);
	33	Adler *et al.*, "Neurophysiological Studies of Sensory Gating in Rats: Effects of Amphetamine, Phencyclidine, and Haloperidol," *Biol. Psychiat.* 21: 787-798 (1986);
	34	Adler *et al.*, "Neurophysiological Evidence for a Defect in Neuronal Mechanisms Involved in Sensory Gating in Schizophrenia," *Biol. Psychiat.* 17: 639-654 (1982);
	35	Albertsen *et al.*, "Construction and characterization of a yeast artificial chromosome library containing seven haploid human genome equivalents," *Proc. Natl. Acad. Sci.* 87: 4256-4260 (1990);
	36	Alkondon and Albuquerque, "Diversity of Nicotinic Acetylcholine Receptors in Rat Hippocampal Neurons. I. Pharmacological and Functional Evidence for District Structural Subtypes," *J. Pharm. Ex. Ther.* 265: 1455-1473 (1993);
	37	Amar *et al.*, "Agonist pharmacology of the neuronal α7 nicotinic receptor expressed in *Xenopus* oocytes," *FEBS* 327: 284-288 (1993);
	38	Anderson and Young, "Quantitative Filter Hybridization," in *Nucleic Acid Hybridization A Practical Approach*, Hames and Higgins (eds.), pp. 73-109, IRL Press (1985);
	39	Barnes, "PCR Amplification of up to 35-kb DNA with high fidelity and high yield from λ bacteriophage templates," *Proc. Natl. Acad. Sci. U.S.A.* 91: 2216-2220 (1994);
	40	Beard *et al.*, "Transcription Mapping of Mouse Adenovirus Type 1 Early Region 3," *Virology*, pp. 75-81 (1990);
	41	Beeson *et al.*, "The human muscle nicotinic acetylcholine receptor α-subunit exists as two isoforms: a novel exon," *EMBO J.* 9: 2101-2106 (1990);
	42	Bender *et al.*, "Evidence that the Packaging Signal of Moloney Murine Leukemia Virus Extends into the *gag* Region," *J. Virol.* 61: 1639-1646 (1987);
	43	Bernstein *et al.*, "Gene Transfer with Retrovirus Vectors," *Genet. Eng.* 7: 235-261 (1985);
	44	Bessis *et al.*, "Negative regulatory elements upstream of a novel exon of the neuronal nicotinic acetylcholine receptor of α2 subunit gene," *Nucl. Acids Res.* 21: 2185-2192 (1993);
	45	Bickford-Wimer *et al.*, "Auditory Sensory Gating in Hippocampal Neurons: A Model System in the Rat," *Biol. Psychiat.* 27: 183-192 (1990);
	46	Bickford and Wear, "Restoration of sensory gating of auditory evoked response by nicotine in fimbria-fornix lesioned rats," *Brain Res.* 705: 235-240 (1995);
	47	Biedler *et al.*, "Multiple Neurotransmitter Synthesis by Human Neuroblastoma Cell Lines and Clones," *Cancer Res.* 38: 3751-3757 (1978);
	48	Blount and Merlie, "Mutational Analysis of Muscle Nicotinic Acetylcholine Receptor Subunit Assembly," *J. Cell Biol.* 111: 2613-2622 (1990);
	49	Boshart *et al.*, "A Very Strong Enhancer is Located Upstream of an Immediate Early Gene of Human Cytomegalovirus," *Cell* 41:521-530 (1985);
	50	Boutros and Overall, "Replication and Extension of P50 Findings in Schizophrenia," *Clin. Electroencephalog.* 22: 40-45 (1991);
	51	Braff *et al.*, "Gating and Habituation of the Startle Reflex in Schizophrenic Patients," *Arch. Gen. Psychiat.* 49: 206-215 (1992);
	52	Breier *et al.*, "National Institute of Mental Health Longitudinal Study of Chronic Schizophrenia, Prognosis and Predictors of Outcome," *Arch. Gen. Psychiat.*, 48: 239-246 (1991);
	53	Brownstein *et al.*, "Isolation of Single-Copy Human Genes from a Library of Yeast Artificial Chromosome Clones," *Science* 244: 1348-1351 (1989);
	54	Burke *et al.*, "Cloning of Large Segments of Exogenous DNA into Yeast by Means of Artificial Chromosome Vectors," *Science* 236: 806-812 (1987);
	55	Calzolari *et al.*, "Psychiatric Disorder in a Familial 15;18 Translocation and Sublocalization of Myelin Basic Protein to 18q22.3," *Am. J. Med. Genet.* 67: 154-161 (1996);

Examiner:	Date Considered:

EXAMINER: Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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Examiner:	Date Considered:

EXAMINER: Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.